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 * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * * *

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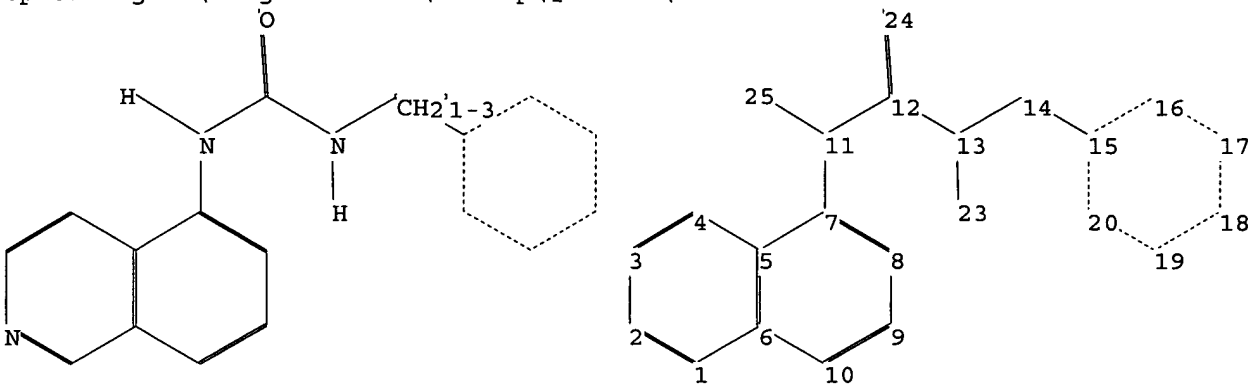


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ring nodes :
1  2  3  4  5  6  7  8  9  10  15  16  17  18  19  20
chain bonds :
7-11  11-12  11-25  12-13  12-24  13-14  13-23  14-15
ring bonds :
1-2  1-6  2-3  3-4  4-5  5-6  5-7  6-10  7-8  8-9  9-10  15-16  15-20  16-17  17-18
 18-19  19-20
exact/norm bonds :
7-11  11-12  12-13  12-24  15-16  15-20  16-17  17-18  18-19  19-20
exact bonds :
11-25  13-14  13-23  14-15
normalized bonds :
1-2  1-6  2-3  3-4  4-5  5-6  5-7  6-10  7-8  8-9  9-10
isolated ring systems :
containing 1 :


Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom
11:CLASS  12:CLASS  13:CLASS  14:CLASS  15:Atom  16:Atom  17:Atom  18:Atom  19:Atom
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L1      STRUCTURE UPLOADED

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L1                STR
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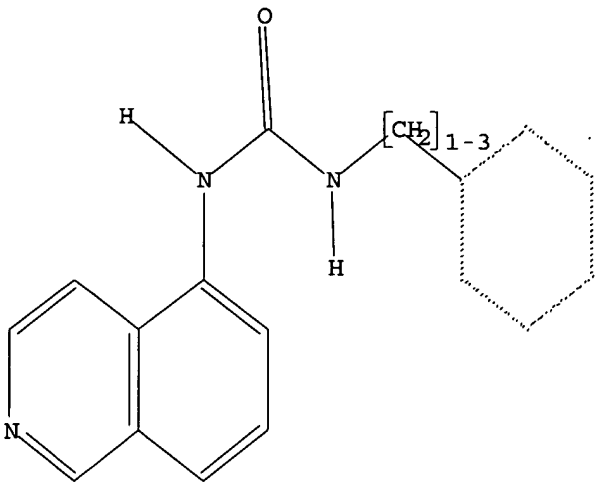

Structure attributes must be viewed using STN Express query preparation.

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L3          260 SEA SSS FUL L1

=> file ca

=> s l3
L4           12 L3

=> d ibib abs fhitstr 1-12
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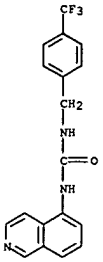
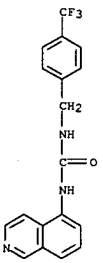
L4 ANSWER 1 OF 12 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 143:241808 CA
TITLE: A-425619 [1-isoquinolin-5-yl-3-(4-trifluoromethylbenzyl)urea], a novel transient receptor potential type V1 receptor antagonist, relieves pathophysiological pain associated with inflammation and tissue injury in rats
AUTHOR(S): Honore, Prisca; Wismer, Carol T.; Mikusa, Joe; Zhu, Chang Z.; Zhong, Chengmin; Gauvin, Donna M.; Gomtsyan, Arthur; El Kouhen, Rachid; Lee, Chih-Hung; Marsh, Kennan; Sullivan, James P.; Faltynek, Connie R.; Jarvis, Michael F.
CORPORATE SOURCE: Neuroscience Research, Global Pharmaceutical Research and Development, Abbott Laboratories, Abbott Park, IL, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2005), 314(1), 410-421
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The vanilloid receptor 1 (VR1, TRPV1), which is a member of the transient receptor potential (TRP) superfamily, is highly localized on peripheral and central processes of nociceptive afferent fibers. Activation of TRPV1 contributes to the pronociceptive effects of capsaicin, protons, heat, and various endogenous lipid agonists such as anandamide and N-arachidonoyl-dopamine. A-425619 is a novel potent and selective antagonist at both human and rat TRPV1 receptors. In vivo, A-425619 dose dependently reduced capsaicin-induced mech. hyperalgesia (ED50 = 45 μmol/kg p.o.). A-425619 was also effective in models of inflammatory pain and postoperative pain. A-425619 potently reduced complete Freund's adjuvant-induced chronic inflammatory pain after oral administration (ED50 = 40 μmol/kg p.o.) and was also effective after either i.t. administration or local injection into the inflamed paw. Furthermore, A-425619 maintained efficacy in the postoperative pain model after twice daily dosing p.o. for 5 days. A-425619 also showed partial efficacy in models of neuropathic pain. A-425619 did not alter motor performance at the highest dose tested (300 μmol/kg p.o.). Taken together, the present data indicate that A-425619, a potent and selective antagonist of TRPV1 receptors, effectively relieves acute and chronic inflammatory pain and postoperative pain.
IT **581809-67-8**, A 425619
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(A-425619, a novel transient receptor potential type V1 receptor antagonist, relieves pathophysiol. pain associated with inflammation and tissue injury in rats)
RN 581809-67-8 CA
CN Urea, N-5-isoquinolinyl-N'-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 12 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 143:241807 CA
TITLE: A-425619 [1-isoquinolin-5-yl-3-(4-trifluoromethylbenzyl)urea], a novel and selective transient receptor potential type V1 receptor antagonist, blocks channel activation by vanilloids, heat, and acid
AUTHOR(S): El Kouhen, Rachid; Surowy, Carol S.; Bianchi, Bruce R.; Neelands, Torben R.; McDonald, Heath A.; Niforatos, Wende; Gomtsyan, Arthur; Lee, Chih-Hung; Honore, Prisca; Sullivan, James P.; Jarvis, Michael F.; Faltynek, Connie R.
CORPORATE SOURCE: Neuroscience Research, Global Pharmaceutical Research and Development, Abbott Laboratories, Abbott Park, IL, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2005), 314(1), 400-409
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The vanilloid receptor transient receptor potential type V1 (TRPV1) integrates responses to multiple stimuli, such as capsaicin, acid, heat, and endovanilloids and plays an important role in the transmission of inflammatory pain. Here, we report the identification and in vitro characterization of A-425619, a novel, potent, and selective TRPV1 antagonist. A-425619 was found to potently block capsaicin-evoked increases in intracellular calcium concns. in HEK293 cells expressing recombinant human TRPV1 receptors (IC50 = 5 nM). A-425619 showed similar potency (IC50 = 3-4 nM) to block TRPV1 receptor activation by anandamide and N-arachidonoyl-dopamine. Electrophysiol. expts. showed that A-425619 also potently blocked the activation of native TRPV1 channels in rat dorsal root ganglion neurons (IC50 = 9 nM). When compared with other known TRPV1 antagonists, A-425619 exhibited superior potency in blocking both naive and phorbol ester-sensitized TRPV1 receptors. Like capsazepine, A-425619 demonstrated competitive antagonism (pA2 = 2.5 nM) of capsaicin-evoked calcium flux. Moreover, A-425619 was 25- to 50-fold more potent than capsazepine in blocking TRPV1 activation. A-425619 showed no significant interaction with a wide range of receptors, enzymes, and ion channels, indicating a high degree of selectivity for TRPV1 receptors. These data show that A-425619 is a structurally novel, potent, and selective TRPV1 antagonist.
IT **581809-67-8**, A 425619
RL: PAC (Pharmacological activity); BIOL (Biological study)
(A-425619 as a potent and selective capsaicin receptor type VR1 antagonist)
RN 581809-67-8 CA
CN Urea, N-5-isoquinolinyl-N'-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)

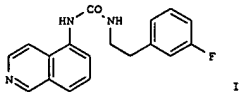


REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 12 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 142:481963 CA
TITLE: Preparation of used azabicyclic compounds that inhibit vanilloid receptor subtype 1 (VR1) receptor
INVENTOR(S): Lee, Chih-Hung; Bayburt, Erol K.; DiDomenico, Stanley; Drizin, Irene; Gomtsyan, Arthur R.; Koenig, John R.; Perner, Richard J.; Schmidt, Robert G.; Turner, Sean C.; Jinkerson, Tammie K.; Zheng, Guo Zhu
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 94 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

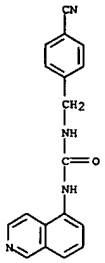
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005113576	A1	20050526	US 2004-911019	20040804
PRIORITY APPLN. INFO.:			US 2003-492528P P	20030805

OTHER SOURCE(S): MARPAT 142:481963
GI

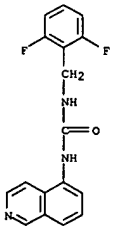


I

AB Azabicyclic compds., such as R-X5-C(:Z1)-Z2-L-R9 [R = substituted or unsubstituted azabicyclyl moiety, such as 5-isoquinolinyl, 4-indazolyl, 4-indolyl or 5-cinnolinyl; X5 = -N(R8a)-, -C(R8a)(R8b)-; Z1 = O, NH, S; Z2 = bond, -NH-, -O-; L = alkylene, alkenylene, alkynylene, cycloalkylene; R8a = H, alkyl; R8b = H, OH, halogen, alkyoxy, alkoxycarbonylalkyl, alkylcarbonyloxy, alkylsulfonyloxy; R9 = aryl], were prepared for use in pharmaceutical compns. as VR1 antagonists for treating a disorder wherein the disorder is ameliorated by inhibiting a VR1 receptor, such as pain, inflammatory thermal hyperalgesia, urinary incontinence and bladder overactivity. Thus, N-[2-(3-fluorophenyl)ethyl]-N'-isoquinolin-5-ylurea (I) was prepared starting from 5-isoquinolinamine, Cl3CCOCl and F-3-C6H4(CH2)2NH2 via urea formation in 65% yield refluxing F-3-C6H4(CH2)2NH2 and 2,2,2-trichloro-N-5-isoquinolinylacetamide in MeCN using DBU. The prepared azabicyclic compds. were tested in vivo to determine their antinociceptive effect in male mice.
IT **581810-26-6P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of fused azabicyclic compds. that inhibit vanilloid subtype 1 (VR1) receptor)
RN 581810-26-6 CA
CN Urea, N-[(4-cyanophenyl)methyl]-N'-5-isoquinolinyl- (9CI) (CA INDEX NAME)



L4 ANSWER 4 OF 12 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 142:456241 CA
TITLE: Design and synthesis of Rho kinase inhibitors (I). [Erratum to document cited in CA141:046759]
AUTHOR(S): Takami, Atsuya; Iwakubo, Masayuki; Okada, Yuji; Kawata, Takehisa; Odai, Hideharu; Takahashi, Nobuaki; Shindo, Kazutoshi; Kimura, Kaname; Tagami, Yoshimichi; Miyake, Mika; Fukushima, Kayoko; Inagaki, Masaki; Amano, Mutsuki; Kaibuchi, Kozo; Iijima, Hiroshi
CORPORATE SOURCE: Pharmaceutical Research Laboratories, Kirin Brewery Co. Ltd, Takasaki-shi, Gunma, 370-1295, Japan
SOURCE: Bioorganic & Medicinal Chemistry (2004), 12(23), 6317
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A sentence is added in the Acknowledgements section: "This work was supported by the grant from the Pharmaceuticals and Medical Devices Agency (PMDA).".
IT **709046-05-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(design and synthesis of Rho kinase inhibitors (Erratum))
RN 709046-05-9 CA
CN Urea, N-[(2,6-difluorophenyl)methyl]-N'-5-isoquinolinyl- (9CI) (CA INDEX NAME)



L4 ANSWER 5 OF 12 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 142:240400 CA
TITLE: Novel transient receptor potential vanilloid 1 receptor antagonists for the treatment of pain: Structure-activity relationships for ureas with quinoline, isoquinoline, quinazoline, phthalazine, quinoxaline, and cinnoline moieties
AUTHOR(S): Gomtsyan, Arthur; Bayburt, Erol K.; Schmidt, Robert G.; Zheng, Guo Zhu; Perner, Richard J.; Didomenico, Stanley; Koenig, John R.; Turner, Sean; Jinkerson, Tammie; Drizin, Irene; Hannick, Steven M.; Macri, Bryan S.; McDonald, Heath A.; Honore, Prisca; Wismer, Carol T.; Marsh, Kennan C.; Wetter, Jill; Stewart, Kent D.; Oie, Tetsuro; Jarvis, Michael F.; Surowy, Carol S.; Faltynek, Connie R.; Lee, Chih-Hung
CORPORATE SOURCE: Global Pharmaceutical Research and Development, Abbott Laboratories, Abbott Park, IL, 60064, USA
SOURCE: Journal of Medicinal Chemistry (2005), 48(3), 744-752
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
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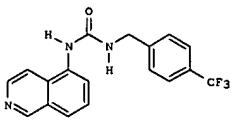
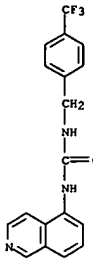


I

AB Transient receptor potential vanilloid 1 (TRPV1) receptor antagonists with various bicyclic heteroarom. pharmacophores were synthesized, and their in vitro activity in blocking capsaicin activation of TRPV1 was assessed. On the basis of the contribution of these pharmacophores to the in vitro potency, they were ranked in the order of 5-isoquinoline > 8-quinoline ≈ 8-quinazoline > 8-isoquinoline ≥ cinnoline ≈ phthalazine ≈ quinoxaline ≈ 5-quinoline. The 5-isoquinoline-containing compound I (hTRPV1 IC50 = 4 nM) exhibited 46% oral bioavailability and in vivo activity in animal models of visceral and inflammatory pain. Pharmacokinetic and pharmacol. properties of I were substantial improvements over the profile of the high-throughput screening hit (hTRPV1 IC50 = 22 nM), which was not efficacious in animal pain models and was not orally bioavailable.
IT **581809-67-8P**
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation, pharmacokinetics, transient receptor potential vanilloid 1

L4 ANSWER 5 OF 12 CA COPYRIGHT 2005 ACS on STN (Continued)
receptor affinity, and structure-activity relationship of isoquinolinyl
trifluoromethylbenzyl urea)
RN 581809-67-8 CA
CN Urea, N-5-isoquinolinyl-N'-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA
INDEX NAME)



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L4 ANSWER 6 OF 12 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 141:174087 CA
TITLE: Preparation of fused azabicyclic compounds that inhibit vanilloid receptor subtype 1 (VR1)
INVENTOR(S): Lee, Chih-Hung; Bayburt, Erol K.; Didomenico, Stanley;
Drizin, Irene; Gomtsyan, Arthur R.; Koenig, John R.; Perner, Richard J.; Schmidt, Robert G.; Turner, Sean C.; White, Tammie K.; Zheng, Guo Zhu
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: U.S. Pat. Appl. Publ., 93 pp., Cont.-in-part of U.S. Ser. No. 364,210.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

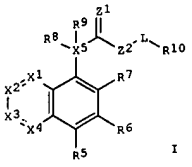
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004157849	A1	20040812	US 2003-634678	20030805
US 6933311	B2	20050823		
US 2003158198	A1	20030821	US 2003-364210	20030211
WO 2005016890	A1	20050224	WO 2004-US25109	20040804

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-364210 A2 20030211
US 2002-358220P P 20020220
US 2003-634678 A 20030805

OTHER SOURCE(S): MARPAT 141:174087
GI

L4 ANSWER 6 OF 12 CA COPYRIGHT 2005 ACS on STN (Continued)



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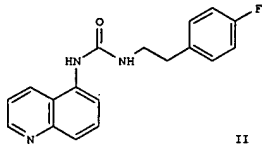
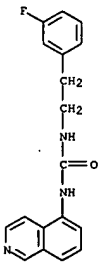
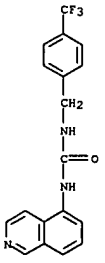


II

AB Compds. of formula I [X1-X5 = (substituted) N, (substituted) CH; Z1 = O, NH, S; Z2 = bond, NH, O; L = alkylene, cycloalkylene, piperazinediyl, etc.; R5-R9 = H, alkyl, alkenyl, alkoxy, carboxy, cycloalkyl, formyl, mercapto, etc.; R10 = H, aryl, cycloalkyl, heterocyclyl] are prepared as vanilloid receptor subtype 1 (VR1) antagonists that are useful in treating pain, inflammatory thermal hyperalgesia, urinary incontinence and bladder overactivity. Thus, II was prepared from 5-aminoisoquinoline and 2-(3-fluorophenyl)ethylamine. The prepared compds. were found to be antagonists of VR1 with IC50 of 0.1 nM to 1000 nM.
IT **581809-65-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of fused azabicyclic compds. as vanilloid receptor 1 inhibitors)
RN 581809-65-6 CA
CN Urea, N-[2-(3-fluorophenyl)ethyl]-N'-5-isoquinolinyl- (9CI) (CA INDEX NAME)



L4 ANSWER 7 OF 12 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 141:157010 CA
TITLE: N-Isoquinolin-5-yl-N'-aralkyl-urea and -amide antagonists of human vanilloid receptor 1
AUTHOR(S): Jetter, Michele C.; Youngman, Mark A.; McNally, James J.; Zhang, Sui-Po; Dubin, Adrienne E.; Nasser, Nadia; Dax, Scott L.
CORPORATE SOURCE: Johnson & Johnson Pharmaceutical Research and Development, Spring House, PA, 19477, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(12), 3053-3056
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:157010
AB Starting from a low micromolar agonist lead identified by high-throughput screening, series of N-isoquinolin-5-yl-N'-aralkyl ureas and analogous amides were developed as potent antagonists of human vanilloid receptor 1 (VR1). The synthesis and structure-activity relationships (SAR) of the series are described.
IT **581809-67-8P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of n-isoquinolin-5-yl-N'-aralkyl-urea and -amide including their structure-activity relationships as antagonists of human vanilloid receptor 1)
RN 581809-67-8 CA
CN Urea, N-5-isoquinolinyl-N'-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)

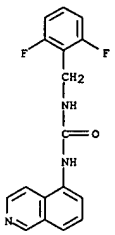


REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L4 ANSWER 8 OF 12 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 141:46759 CA
TITLE: Design and synthesis of Rho kinase inhibitors (I)
AUTHOR(S): Takami, Atsuya; Iwakubo, Masayuki; Okada, Yuji; Kawata, Takehisa; Odai, Hideharu; Takahashi, Nobuaki; Shindo, Kazutoshi; Kimura, Kaname; Tagami, Yoshimichi; Miyake, Mika; Fukushima, Kayoko; Inagaki, Masaki; Amano, Mutsuki; Kaibuchi, Kozo; Iijima, Hiroshi
CORPORATE SOURCE: Pharmaceutical Research Laboratories, Kirin Brewery Co. Ltd., Gunma, Takasaki-shi, 370-1295, Japan
SOURCE: Bioorganic & Medicinal Chemistry (2004), 12(9), 2115-2137
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:46759

AB Several structurally unrelated scaffolds of the Rho kinase inhibitor were designed using pharmacophore information obtained from the results of a high-throughput screening and structural information from a homol. model of Rho kinase. A docking simulation using the ligand-binding pocket of the Rho kinase model helped to comprehensively understand and to predict the structure-activity relationship of the inhibitors. This understanding was useful for developing new Rho kinase inhibitors of higher potency and selectivity. We identified several potent platforms for developing the Rho kinase inhibitors, namely, pyridine, 1H-indazole, isoquinoline, and phthalimide.

IT **709046-05-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(design and synthesis of Rho kinase inhibitors)
RN 709046-05-9 CA
CN Urea, N-[(2,6-difluorophenyl)methyl]-N'-5-isoquinolinyl- (9CI) (CA INDEX NAME)



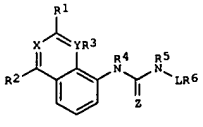
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS

L4 ANSWER 8 OF 12 CA COPYRIGHT 2005 ACS on STN (Continued)
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 12 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 140:111290 CA
TITLE: Preparation of naphthalenylureas, quinolinylureas, and isoquinolinylureas as modulators of vanilloid VR1 receptor ligands.
INVENTOR(S): Codd, Ellen; Dax, Scott L.; Jetter, Michele; Mcdonnell, Mark; Mcnally, James J.; Youngman, Mark
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 205 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004007459	A2	20040122	WO 2003-US21518	20030710
WO 2004007459	A3	20040318		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004157865	A1	20040812	US 2003-616579	20030710
PRIORITY APPLN. INFO.:			US 2002-395728P	P 20020712
			US 2002-395951P	P 20020715

OTHER SOURCE(S): MARPAT 140:111290
GI

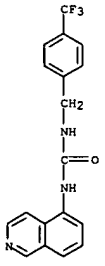


I

AB Title compds. [I; R1, R2 = H, OH, halo, (substituted) alkyl, alkoxy, alkylthio, cycloalkyl, cycloalkoxy, etc.; R3 = H, OH, F, Cl, NO2, amino; L = (substituted) alkylene; R4, R5 = H, alkyl; R6 = (substituted) Ph, naphthyl, heteroaryl, cycloalkyl, heterocyclyl; X = CH, N, NO; Y = C, N; Z = O, S], were prepared as potent antagonists or agonists of VR1 which are useful for the treatment and prevention of inflammatory and other pain.

L4 ANSWER 9 OF 12 CA COPYRIGHT 2005 ACS on STN (Continued)
Thus, (1-chloroisoquinolin-5-yl)carbamic acid Ph ester and 4-trifluoromethylbenzylamine were stirred overnight in DMSO to give 61% 1-(1-chloroisoquinolin-5-yl)-3-(4-trifluoromethylbenzyl)urea. I bound to VR1 receptors with Ki = 0.10-100,000 nM.

IT **581809-67-8P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of naphthalenylureas, quinolinylureas, and isoquinolinylureas as modulators of vanilloid VR1 receptor ligands)
RN 581809-67-8 CA
CN Urea, N-5-isoquinolinyl-N'-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)

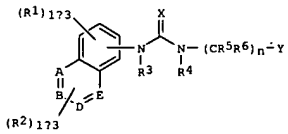


L4 ANSWER 10 OF 12 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 139:292162 CA
TITLE: Heteroaromatic ureas as vanilloid receptor (VR1) modulators, in particular antagonists, for treating pain and/or inflammation
INVENTOR(S): Brown, Rebecca Elizabeth; Doughty, Victoria Alexandra; Hollingworth, Gregory John; Jones, A. Brian; Lindon, Matthew John; Moyes, Christopher Richard; Rogers, Lauren
PATENT ASSIGNEE(S): Merck Sharp & Dohme Limited, UK
SOURCE: PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003080578	A1	20031002	WO 2003-GB1302	20030321
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2479150	AA	20031002	CA 2003-2479150	20030321
EP 1490340	A1	20041229	EP 2003-710014	20030321
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2005107388	A1	20050519	US 2003-505358	20030321
JP 2005526798	T2	20050908	JP 2003-578333	20030321

PRIORITY APPLN. INFO.: GB 2002-6876 A 20020322
WO 2003-GB1302 W 20030321

OTHER SOURCE(S): MARPAT 139:292162
GI



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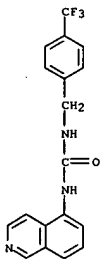
L4 ANSWER 10 OF 12 CA COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 12 CA COPYRIGHT 2005 ACS on STN (Continued)

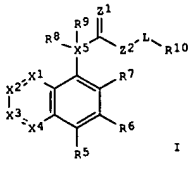
AB Title compds. I (wherein A, B, D, E are each C or N with the proviso that one or more are N; R1, R2 = independently H, halo, alk(enyl/ynyl), haloalkyl, hydroxyalkyl, cycloalkyl, cycloalkylalkyl, NH2 and derivs., CO2H and derivs., (un)substituted alkyl, alkoxy; R3, R4 = independently H, alk(en/yn)yl; R5, R6 = at each occurrence, independently H, alk(enyl/ynyl), alkoxy, acyloxy, carboxy and derivs., CONH2 and derivs., sulfonyl(alkyl/amino), aryl, hetero(aryl/cyclyl), (un)substituted alkyl; or CR5R6 = 3-6 carbocyclic membered ring; R7, R8 = at each occurrence, independently H, alk(en/yn)yl, cycloalkyl, fluoroalkyl; or NR7R8 = (un)substituted 4-7 heteroaliph. membered ring; X = O, S or =NCN; Y = aryl, heteroaryl, carbocyclyl, fused carbocyclyl group; n = 0, 1, 2, 3; and their pharmaceutically acceptable salts, N-oxides, and prodrugs] were prepared as vanilloid receptor (VR1) modulators, in particular antagonists, for treating conditions or diseases in which pain and/or inflammation predominates. For example, 1-isoquinolin-5-yl-3-(3-phenylpropyl)urea was prepared by reacting isoquinoline-5-carboxylic acid with diphenylphosphoryl azide in toluene at reflux for 1 h through a Curtius rearrangement, followed by addition of 3-phenylpropylamine and reflux for 18 h. I bound to the VR1 receptor with an IC50 < 1 μM, and in the majority of cases, < 200 nM. I are predominantly VR1 antagonists with a few of them VR1 partial antagonists and VR1 partial agonists. Thus, I and their pharmaceutical compns. are useful for treating pain and/or inflammation.
IT 581809-67-8P, 1-Isoquinolin-5-yl-3-[4-(trifluoromethyl)benzyl]urea
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(VR1 receptor ligand; preparation of heteroarom. ureas as vanilloid receptor modulators for treating pain and inflammation)
RN 581809-67-8 CA
CN Urea, N-5-isoquinolinyl-N'-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 11 OF 12 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 139:197383 CA
TITLE: Preparation of fused azabicyclic compounds that inhibit vanilloid receptor subtype 1 (VR1)
INVENTOR(S): Lee, Chih-Hung; Bayburt, Erol K.; Didomenico, Stanley; Drizin, Irene; Gomtsyan, Arthur R.; Koenig, John R.; Perner, Richard J.; Schmidt, Robert G.; Turner, Sean C.; White, Tammie K.; Zheng, Guo Zhu
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 79 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003158198	A1	20030821	US 2003-364210	20030211
CA 2476936	AA	20030828	CA 2003-2476936	20030211
WO 2003070247	A1	20030828	WO 2003-US4187	20030211
W: CA, JP, MX				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR				
EP 1478363	A1	20041124	EP 2003-716014	20030211
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2004157849	A1	20040812	US 2003-634678	20030805
US 6933311	B2	20050823		
US 2004209884	A1	20041021	US 2004-842311	20040510

PRIORITY APPLN. INFO.: US 2002-358220P P 20020220
US 2002-79324 A 20020220
US 2003-364210 A 20030211
WO 2003-US4187 W 20030211

OTHER SOURCE(S): MARPAT 139:197383
GI



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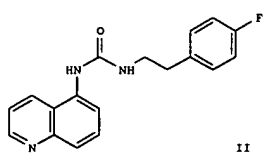


II

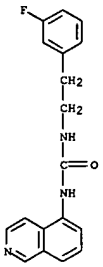
AB Compds. of formula I [X1-X5 = (substituted) N, (substituted) CH; Z1 = O, NH, S; Z2 = bond, NH, O; L = alkylene, cycloalkylene, piperazinediyl, etc.; R5-R9 = H, alkyl, alkenyl, alkoxy, carboxy, cycloalkyl, formyl,

L4 ANSWER 11 OF 12 CA COPYRIGHT 2005 ACS on STN (Continued)
mercapto, etc.; R10 = H, aryl, cycloalkyl, heterocyclyl] are prepd. as vanilloid receptor subtype 1 (VR1) antagonists that are useful in treating
pain, inflammatory thermal hyperalgesia, urinary incontinence and bladder overactivity. Thus, II was prepd. from 5-aminoisoquinoline and 2-(3-fluorophenyl)ethylamine. The prepd. compds. were found to be antagonists of VR1 with IC50 of.1 nM to 1000 nM.

IT **581809-65-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of fused azabicyclic compds. as vanilloid receptor 1 inhibitors)

RN 581809-65-6 CA

CN Urea, N-[2-(3-fluorophenyl)ethyl]-N'-5-isoquinolinyl- (9CI) (CA INDEX NAME)



L4 ANSWER 12 OF 12 CA COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 139:197382 CA

TITLE: Preparation of isoquinolines, indoles, and related compounds as antagonists of vanilloid receptor subtype
1 (VR1).

INVENTOR(S): Lee, Chih-Hung; Bayburt, Erol K.; Didomenico, Stanley;
Drizin, Irene; Gomtsyan, Arthur R.; Koenig, John R.; Perner, Richard J.; Schmidt, Robert G.; Turner, Sean C.; White, Tammie K.; Zheng, Guo Zhu

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 38 pp.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003158188	A1	20030821	US 2002-79324	20020220
CA 2476936	AA	20030828	CA 2003-2476936	20030211
WO 2003070247	A1	20030828	WO 2003-US4187	20030211
W: CA, JP, MX				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR				
EP 1478363	A1	20041124	EP 2003-716014	20030211
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

PRIORITY APPLN. INFO.:
US 2002-79324 A 20020220
US 2003-364210 A 20030211
WO 2003-US4187 W 20030211

OTHER SOURCE(S): MARPAT 139:197382

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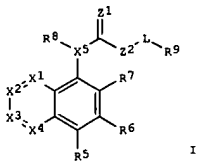


I

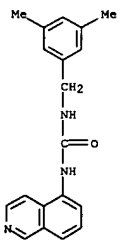
L4 ANSWER 12 OF 12 CA COPYRIGHT 2005 ACS on STN (Continued)

AB Title compds. [I; X1 = N, CR1; X2 = N, CR2; X3 = N, NR3, CR3; X4 = null, N, CR4; X5 = N, CH2; Z1 = O, NH, S; Z2 = NH, O; L = piperazinylene, alkenylene, alkylene, alkynylene, cycloalkylene, (CH2)mO(CH2)n, NHO, NHNH;
m, n = 1-6; R1, R3, R5, R6, R7 = H, alkenyl, alkoxy, alkoxyalkoxy, alkoxyalkyl, alkoxycarbonyl, alkoxycarbonylalkyl, A, ACO, ACOA, ACO2, AS, alkynyl, CO2H, ACO2H, cyano, cyanoalkyl, cycloalkyl, cycloalkylalkyl, ethylenedioxy, CHO, ACHO, haloalkoxy, haloalkyl, haloalkylthio, halo, OH, HOA, methylenedioxy, SH, ASH, NO2, (CF3)2(HO)C, NRASO2RB, SO2ORA, SO2RB, NZAZB, (NZAZB)A, (NZAZB)CO, (NZAZB)COA, (NZAZB)SO2; ZA, ZB = H, A, ACO, CHO, aryl, aralkyl; R2, R4 = H, alkenyl, AO, alkoxyalkoxy, AOA, AO2C, AO2CA, A, ACO, ACOA, ACO2, AS, alkynyl, CO2H, carboxyalkyl, cyano, cyanoalkyl, cycloalkyl, cycloalkylalkyl, ethylenedioxy, CHO, ACHO, haloalkoxy, haloalkyl, haloalkylthio, halo, OH, HOA, methylenedioxy, SH, HSA, NO2, (CF3)2(HO)C, NRAS(O)2RB, SO2ORA, SO2RB, NZAZB, (NZAZB)alkyl, (NZAZB)ACO, (NZAZB)CO, (NZAZB)COA, (NZAZB)SO2, (NZAZB)C(:NH), (NZAZB)C(:NCN)NH, (NZAZB)C(:NH)NH: RA = H, A; RB = A, aryl, aralkyl; R8 = null, H, A; R9 = H, aryl; heterocycle; A = alkyl; dotted line = optional double bond], were prepared for treating pain, inflammatory thermal hyperalgesia, urinary incontinence and bladder overactivity (no data). Thus, 2,2,2-trichloro-N-isoquinolin-5-ylacetamide, (preparation given) DBU, and
2-(3-fluorophenyl)ethylamine in acetonitrile were refluxed for 10 h to give 65% N-[2-(3-fluorophenyl)ethyl]-N'-isoquinolin-5-ylurea.

IT **581810-09-5P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(claimed compound; preparation of isoquinolines, indoles, and related compds.
as antagonists of vanilloid receptor subtype 1)

RN 581810-09-5 CA

CN Urea, N-[(3,5-dimethylphenyl)methyl]-N'-5-isoquinolinyl- (9CI) (CA INDEX NAME)



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L3          260 S L1 FULL

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L4           12 S L3

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---Logging off of STN---


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Executing the logoff script...


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STN INTERNATIONAL LOGOFF AT 10:51:26 ON 27 OCT 2005
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